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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,105	BURCHELL ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9 and 12-15* is/are rejected.

7)☒ Claim(s) *3-7 and 12-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/24/06 has been entered.

2. Applicant's response to the Final Office Action mailed August 23, 2005 is acknowledged (paper filed 2/24/06). Currently, claims 2-7, 9, and 12-15 are under consideration.

3. Rejections and/or Objections of record not reiterated herein have been withdrawn.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

5. The Information Disclosure Statements filed 11/28/05 has been considered as to the merits.

Claim Objections

6. Claims 3-7 and 12-15 are objected to because of the following informalities: The claims start with "A", however the accurate claim beginning should be "The". Please modify the claims for proper claim format. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The terms "fragment and derivative thereof" in claim 12 are relative terms, which renders the claim indefinite. The term "fragment and derivative thereof" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what if any fragments and/or derivatives would maintain the activity of the antibody set forth in the claims. Accordingly the claim is not clear.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The written description in this case only sets forth antibodies generated against adult liver components or components (antigens) consisting of rat liver testosterone/4-nitrophenol UDPGT on page 18, the microsomal glucose-6-phosthate system, T2, and T3 on page 19 and 20, niethyl-moximate PGEM (PGEM-MOX) on page 19, PGE_2 on page 19, cytochrome P450s on page 20; therefore claim 12 drawn to "fragments and derivatives thereof" has not been described in the specification. The written description is not commensurate in scope with the claims drawn to "fragments and derivatives thereof" with respect to the claimed antibodies (binding moiety).

There is no guidance as to what "fragments and derivatives thereof" would work in the claimed method or how much derivation can occur while retaining the required product characteristics necessary to be considered a "fragments and derivatives thereof", further reading on the instantly claimed method. In other words the "fragments and derivatives thereof" must retain the appropriate properties allowing for fetal cell separation.

There is no guidance as to what the "fragments and derivatives thereof" can or cannot be used in the method being claimed. The specification does not include structural examples of "fragments and derivatives thereof". Thus, the resulting "fragments and derivatives thereof" could result in a complexes not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The skilled artisan cannot envision the detailed structure of the "fragments and derivatives thereof", thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Therefore the full breadth of the claim does not meet the written description provision of 35 USC 112, first paragraph.

No disclosure, beyond the antibodies to rat liver testosterone/4-nitrophenol UDPGT on page 18, the microsomal glucose-6-phosthate system, T2, and T3 on page 19 and 20, niethyl-moximate PGEM (PGEM-MOX) on page 19, PGE_2 on page 19, cytochrome P450s on page 20 are made in the specification. This is insufficient to support the claims drawn to the fragments and derivatives thereof as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore the full breadth of the claims does not meet the written description provision of 35 USC 112, first paragraph.

9. Claims 9 and 12-15 (*with respect to claims 12-15 depending on claim 9)* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of separating fetal or embryonic cells from maternal blood cells utilizing an anti-GLUT2 antibody conjugate (see pages 23-25 of the specification), this does not reasonably provide enablement for fetal/embryonic cell separation with any and all antibodies directed to the various recited components included in claim 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specifically, the specification discloses the production of several antibody conjugates to bind to rat liver testosterone/4-nitrophenol UDPGT on page 18, the microsomal glucose-6-phosthate system, T2, and T3 on page 19 and 20, niethyl-moximate PGEM (PGEM-MOX) on page 19, PGE_2 on page 19, cytochrome P450s on page 20.

However, the mere generation of antibodies does not adequately exemplify that these same antibodies will necessarily bind fetal cells (the fetal cells may not have the antigen) or that the corresponding antigens to the generated antibodies are expressed differentially in fetal/embryonic cells allowing for separation from maternal blood cells.

The prior art has taught that various antibodies can be constructed but they are not always useful in the separation of fetal/embryonic cells in a maternal blood cell sample. In particular, the antigens are not always expressed, if expressed they are not always differentially expressed in fetal/embryonic cells when compared with maternal cells or other cell types which may be found in the sample, or the antibody may not be sensitive enough to detect the fetal cell population. See Huie et al. (PNAS, 2/27/01, Vol.98, No.5, pages 2682-2687) and Leschot (Early Human Development Vol.47, Supplemental, 1996, pages S69-S72).

Accordingly, claim 9 is enabling for a method of separating fetal or embryonic cells from maternal blood cells utilizing an anti-GLUT2 antibody conjugate, but not for any and all components recited in the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 9, 12, 14 and 15 (*with respect to claims 12, 14 and 15 depending on claim 9*) are rejected under 35 U.S.C. 102(b) as being anticipated by Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993).

Bianchi et al. teach a method of isolating fetal nucleated cells from maternal blood. An antigen present on the cell surface of the fetal erythrocyte is detected and related to a gene or gene portion associated with a disease or condition, a chromosomal abnormality or sex-specific DNA, in the maternal blood sample. See abstract.

Three different antibodies are utilized to separate the fetal nucleated erythrocytes (red blood cells) form maternal blood. These antibodies are anti-CD 71, anti-CD 36, and anti-GPA. Anti-CD 71 binds the transferrin receptor, CD-36 binds the thrombospondin receptor (hormone receptor), while anti-GPA binds glycophorin A (glycoprotein). See page 294 4th paragraph. Blood samples were collected from pregnant women between 8 and 19 weeks gestation (within the first trimester). See page 295 1st paragraph.

In the method, cells were isolated/separated by antibody binding and analyzed via flow cytometry, sorting, and PCR. See page 295 through 296. The results showed that the GPA (red cell-specific antigen) allowed for the separation of fetal nucleated erythroid cells from maternal blood. See page 299 last paragraph.

Claim Rejections - 35 USC § 103

II. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claim 13 (*with respect to claim 13 depending on claim 9*) is rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Bianchi et al. as set forth above.

Bianchi et al. differs from the instant invention in not specifically teaching reagent immobilization to a solid support such as micro titer plates.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the reagents on a solid support/micro titer plates as taught by Maggio in the assay method to isolate red blood cells of Bianchi et al. because Maggio taught that micro plates or micro titer plates "are very convenient for reagent immobilization and eliminate washing thereby reducing labor in assay procedures". Page 186, last line.

III. Claims 2-7, 12, and 14-15 (*with respect to claims 12, 14 and 15 depending on claim 2*) are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770).

Bianchi et al. teach a method of isolating fetal nucleated cells from maternal blood. An antigen present on the cell surface of the fetal erythrocyte is detected and related to a gene or gene portion associated with a disease or condition, a chromosomal abnormality or sex-specific DNA, in the maternal blood sample. See abstract.

Three different antibodies are utilized to separate the fetal nucleated erythrocytes (red blood cells) form maternal blood. These antibodies are anti-CD 71, anti-CD 36, and anti-GPA. Anti-CD 71 binds the transferrin receptor, CD-36 binds the thrombospondin receptor (hormone receptor), while anti-GPA binds glycophorin A (glycoprotein). See page 294 4th paragraph.

Blood samples were collected from pregnant women between 8 and 19 weeks gestation (within the first trimester). See page 295 1st paragraph. In the method, cells were isolated/separated by antibody binding and analyzed via flow cytometry, sorting, and PCR. See page 295 through 296. The results showed that the GPA (red cell-specific antigen) allowed for the separation of fetal nucleated erythroid cells from maternal blood. See page 299 last paragraph.

Bianchi et al. differs from the instant invention in failing to teach a method of identifying and isolating embryonic or fetal red blood cells via an adult liver component that is cell surface exposed.

It is noted that the specification teaches that glucose-6-phosphase is an adult liver component meeting the limitations of the claims. (Page 8 section 0047). The references to Hume et al. disclose the use of antibodies to glucose-6-phosphase.

Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) show that the microsomal glucose-6-phosphatase enzyme protein is expressed in human embryonic and fetal red blood cells. Glucose-6-phosphatase was found to be immunopositive for circulating red cells in the primitive megaloblastic series.

Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) et al. teaches that microsomal glucose-6-phosphatase catalyzes the terminal step of glycogenolysis and gluconeogenesis and is expressed predominantly in the liver. The study of the endoplasmic reticulum system involving glucose-6-phosphatase, lead investigators to study other endoplasmic reticulum proteins.

These proteins included uridine diphosphate-glucuronosyltransferase, cytochrome P450 isozymes, nicotinamide adenine dinucleotide phosphatecytochrome P450 oxidoreductase, and prostaglandin H synthase.

Bianchi et al., Hume et al., and Hume et al., are all analogous art because they are from the same field of endeavor, all three inventions teach immunoassay techniques involving fetal red blood cells and prenatal diagnosis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the specific proteins relating to microsomal glucose-6-phosphatase as taught by Hume et al., and Hume et al. in the methods of Bianchi et al. to perform fetal red blood cell identification, isolation, and assay techniques, because Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) taught that the predominantly hepatic protein (glucose-6-phosphatase) in adults is present in nucleated embryonic and fetal red blood cells and is useful in diagnosis of disorders associated with liver protein expression in the first trimester maternal circulation.

While, Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) taught that expression of these key enzymes (glucose-6-phosphatase) in early fetal RBCs provides a means for the study of fetal development in these areas. See abstract.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible treatment and early preparation/education of the fetal family for the birth of an abnormal baby.

With respect to claim 7 wherein the concentration of the detectable adult liver component is at less than 1 percent per cell basis in maternal cells. Such detection limits are viewed as mere assay optimization. Absent results to the contrary or unexpected results the modification is viewed as an obvious modification that does not render the claims patentably distinct from the prior art assay methods.

IV. Claim 13 (*with respect to claims 13 depending on claim 2*) is rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) as applied to claims 2, 5-7, 9 and 14-15 above, and further in view of in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Bianchi et al. in view of Hume et al. and Hume et al. as set forth above.

Bianchi et al. in view of Hume et al. and Hume et al. differ from the instant invention in not specifically teaching reagent immobilization to a solid support such as micro titer plates.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the reagents on a solid support/micro titer plates as taught by Maggio in the assay method to isolate red blood cells of Bianchi et al. in view of Hume et al. and Hume et al. because Maggio taught that micro plates or micro titer plates "are very convenient for reagent immobilization and eliminate washing thereby reducing labor in assay procedures". Page 186, last line.

6. For reasons aforementioned, no claims are allowed.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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